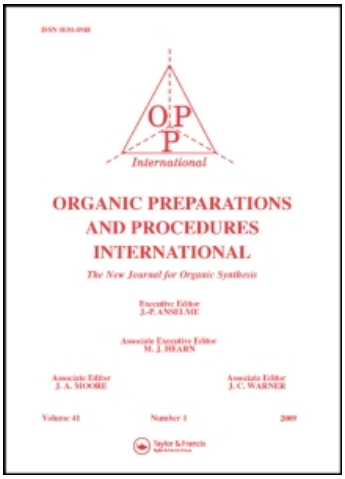

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

FACILE CHROMONE RING-OPENING OF KHELLIN

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To cite this Article Al-Farhan, Emile , Keehn, Philip M. and Stevenson, Robert(1991) 'FACILE CHROMONE RING-OPENING OF KHELLIN', Organic Preparations and Procedures International, 23: 5, 665 — 667
To link to this Article: DOI: 10.1080/00304949109457923
URL: http://dx.doi.org/10.1080/00304949109457923

amount was recrystallized from hexanes to provide white crystals, mp. 38-40°.
FAB MS. MH^+ 207. ^1H NMR ($CDCl_3$): δ 2.78 (s, 2H, $-CH_2CO-$), 3.03 (d, 2H, $-CH_2Ar$), 3.15 (d, 2H, $-CH_2Ar$), 3.61 (s, 1H, OH), 3.77 (s, 3H, OCH_3), 7.13-7.24 (m, 4H, Ar).

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 70.18; H, 6.84

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FACILE CHROMONE RING-OPENING OF KHELLIN

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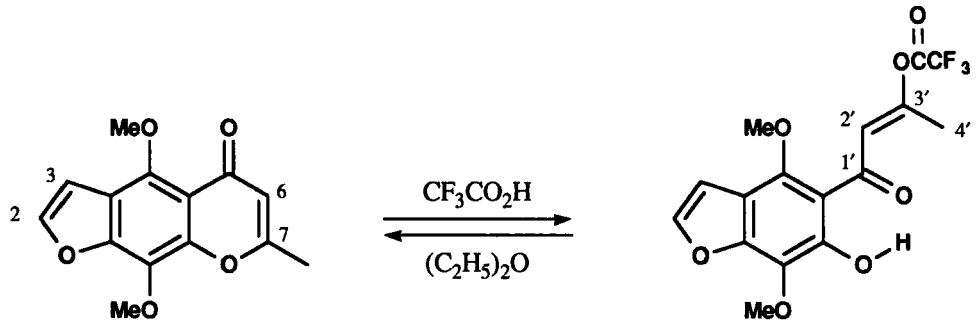
The natural furochromone, khellin (**1**) has long attracted attention on account of vasodilator action, and more recently lipid-altering and antiatherosclerotic activity has been discovered.[1]

We have found that under very mild conditions (chloroform solution containing trifluoroacetic acid at room temperature), khellin (**1**) is transformed quantitatively into a bright yellow crystalline product whose ^1H NMR spectrum retained all proton functionality of the starting furochromone. The diketone enol trifluoroacetate structure (**2**) assigned to this product is supported by empirical analysis ($C_{16}H_{13}F_3O_7$) and ^1H and ^{13}C spectra.[2] Enhancement of the 6-H and 7-Me



1 2

signals of **1** by appropriate irradiation in NOE difference spectra is absent in **2** supporting the 2'-E configuration of the latter.

The ease of heterocycle ring opening (**1** → **2**) is matched by the facility of re-cyclization. Although (**2**) is readily crystallized from benzene, attempted recrystallization from diethyl ether caused immediate loss of the yellow color and yielded khellin, presumably by intramolecular Michael-type addition and trifluoroacetate elimination. It is suggested that this ready **1**⇌**2** transformation may provide useful recognition of chromone functionality.

EXPERIMENTAL SECTION

Melting points were determined on a Hoover capillary melting point apparatus. UV spectra were recorded on a Varian DMS UV-visible spectrophotometer. NMR measurements were carried out on a Varian XL-300 spectrometer operating at 300 MHz for ^1H and 75 MHz for ^{13}C with TMS as internal standard.

Action of Trifluoroacetic Acid on Khellin (1).- Khellin (100 mg) was added to a solution (3 ml) of trifluoroacetic acid in chloroform (10% v/v). The solution, which turned immediately orange and then red, was allowed to stand at room temperature for 3-5 hrs, then evaporated under reduced pressure. Crystallization of the residue from benzene gave 6-*hydroxy*-4,7-*dimethoxy*-5-(3'-*trifluoroacetyloxybut*-2'-(*E*)-*enoyl*)*benzofuran* (**2**) as bright yellow needles, mp. 112-113°; $\lambda_{max}(CHCl_3)$: 327 (log ε 3.15) and 277 nm (log ε 3.15). ^1H NMR ($CDCl_3$): δ 2.49 (br s, 3H, H-4'), 4.09 (s, 3H, OMe), 4.21 (s, 3H, OMe), 6.36 (br s, 1H, H-2'), 7.06 (d, 1H, J = 2.3 Hz, H-3), 7.68 (d, 1H, J = 2.3 Hz, H-2), and 13.12 (s, 1H, phenolic OH). ^{13}C NMR ($CDCl_3$): δ 20.2 (C-4'), 61.4 (OMe), 62.0 (OMe), 105.2 (C-3), 109.1 (C-2'), 111.8 (C-5), 115.0 (q, J = 286 Hz, CF_3), 119.2 (C-3a), 129.6 (C-7), 145.9 (C-2), 146.9 (C-6), 147.4 (C-4), 149.5 (C-7a), 158.9 (q, J = 41 Hz, $\underline{C}OCF_3$), 167.0 (C-3') and 180.5 (C-1').

Anal. Calcd. for $C_{16}H_{13}F_3O_7$: C, 51.34; H, 3.50. Found: C, 51.27; H, 3.50

Transformation of Enol Ester (2) to Khellin (1).- Addition of diethyl ether to the yellow solid (**2**) caused immediate fading. Warming to dissolve and allowing to crystallize gave khellin (**1**) as small

fine needles, mp. 150-152°; lit.[3] mp. 153°, identified additionally by ^{1}H NMR comparison.

Acknowledgement.- We are grateful to Merck, Sharp and Dohme Research Laboratories for a grant which supported this work.

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A NEW METHOD FOR THE SYNTHESIS OF 3β-HYDROXY-4α-BROMOCARANE AND OF *cis*-3-CARENE EPOXIDE

Submitted by (03/04/91)

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The objective of our research was to synthesize 3β-hydroxy-4α-bromocarane. Both *cis*-3-carene epoxide and 3β-hydroxy-4α-bromocarane are important starting materials in the synthesis of some pyrethroids[1,2] and in terpene chemistry.[6] A synthesis of 3β-hydroxy-4α-bromocarane using N-bromosuccinimide and 3-carene has been reported.[3] The reactions of 3α,4α-epoxycarane with HBr resulted in formation of 3β-bromo-4α-hydroxycarane while 3β,4β-epoxycarane gave a mixture of 3α-bromo-4β-hydroxycarane and 3α-hydroxy-4α-bromocarane.[4]

Using a method for the synthesis of trimethylethylene bromohydrin reported in 1944,[5] we found that the synthesis of *trans*-3β-hydroxy-4α-bromocarane can be easily achieved by titration of a mixture of 3-carene and water with an aqueous solution of bromine and potassium bromide at room temperature until the reaction mixture is light orange in color. If the addition is stopped before obtaining this color, 3-carene does not react completely. The reaction product was recrystallized from hexane to yield pure *trans*-3β-hydroxy-4α-bromocarane in 52% yield. ^{1}H NMR analysis of the crude reaction product indicated that the rest of the material corresponds to 3β-hydroxy-4α-bromocarane and 3,4-dibromocarane which can easily be converted back to 3-carene; no attempts were made to